CHO

Cocaine

WIN 35,428

2ß-Carbomethoxy-3β-(3,4-dichlorophenyl)-bicyclo[3.2.1]octane

2B-Carbomethoxy-3β-(3,4-dichlorophenyl)-6B-hydroxy-8-methyl-8-azabicyclo[3.2.1]octane

2β-Carbomethoxy-3β-(3,4-dichlorophenyl)-8-oxabicyclo[3.2.1]octane

2B-Carbomethoxy-3B-(3,4-dichlorophenyl)-7B-hydroxy-8-methyl-8-azabicyclo{3.2.1}octane

Figure 1. Structures of Lead Bicyclo[3.2.1] octanes

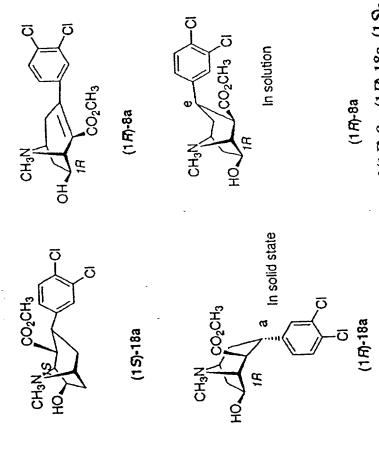


Figure 2. Absolute Configurations of (1*R*)-8a, (1*R*)-18a, (1*S*)-18a

Figure 3

Scheme 1. Synthetic Route to 2,3-Unsaturated Tropanes\*

Ar: a = 3,4-Cl<sub>2</sub> phenyl b = 2-Naphthyl c = 4-F-phenyl d =Phenyl

<sup>a</sup> Reagents: (i) H<sub>2</sub>NCH<sub>3</sub>; (ii) CH<sub>2</sub>(OCH<sub>3</sub>)<sub>2</sub>, pTSA; (iii) NaN(TMS)<sub>2</sub>, PhNTf<sub>2</sub>; (iv) Pd<sub>2</sub>(dba)<sub>3</sub>, ArB(OH)<sub>2</sub>; (v) TMSBr.

3 a. 6-MOM b. 7-MOM

Scheme 2. Synthetic Route to Bridge Oxygenated Tropanes<sup>a</sup>

 $^{a}$  Reagents: (i) SmI<sub>2</sub>; (ii) TMSBr, CH<sub>2</sub>Cl<sub>2</sub>; (iii) N·CH<sub>3</sub>-morpholine-N·oxide, tetra-n-propylammoniumperruthenate.

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Scheme 3. Synthetic Route to Bridge Oxygenated 2-Keto Tropanes<sup>a</sup>

12a

CON(CH<sub>3</sub>)OOH<sub>3</sub> COC2H5 **5**6 25 **(E)** CH3 N € CHan MOMO SE SE MOMO CON(CH3)OCH3 COC2H<sub>5</sub>  $\equiv$ € 22 <del>1</del>1a  $\equiv$ 72 SE HO CH3 N MOMO MOMO

<sup>8</sup>Reagents: (i) HN(CH<sub>3</sub>)OCH<sub>3</sub> A1(CH<sub>3</sub>)<sub>3</sub>; (ii) ETMgBR; (iii) TMSBR, CH<sub>2</sub>Cl<sub>2</sub>.

Scheme 4. Resolution of 8A, 15A, and 18Aª

Figure 7

Scheme 5. Inversion at C6 and C7a

30a: 6-OH (30b: 7-OH)

<sup>a</sup> Reagents: (i) C<sub>6</sub>H<sub>5</sub>COOH, Ph<sub>3</sub>P, DEAD; (ii) LiOH, THF.

Figure 8

Scheme 6. Synthesis of Diarylmethoxy Tropanes<sup>a</sup>

<sup>a</sup> Reagents: (i) NaBH<sub>4</sub>; (ii) 4,4'-difluorobenzhydrol, pTSA.